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Food and Drug Administration
5630 Fishers Lane, Room 1061
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Re: Docket No. 2004N–0081
Use of Materials Derived from Cattle in Human Food and Cosmetics: Interim Final Rule (69 Fed. Reg. 42256; July 14, 2004)

Comments of the Gelatin Manufacturers Institute of America and the Gelatin Manufacturers of Europe

To Whom It May Concern:

The Gelatin Manufacturers Institute of America (GMIA) is a trade association whose members include all of the producers of gelatin in the United States and Canada, and one of the largest Mexican manufacturers. The Gelatin Manufacturers of Europe (GME) represents the nine largest European manufacturers that account for 96% of European gelatin production and approximately 45 percent of worldwide gelatin production. GMIA and GME submit the following comments on the above-referenced interim final rule.

The Gelatin Manufacturers Association of Asia Pacific, the Gelatin Manufacturers Association of Japan, and the South American Gelatin Manufacturing Association have informed us that they concur with these comments.

Gelatin is made from several different types of animal-origin raw materials. The comments in this document pertain only to gelatin made from bovine raw materials.

COMMENT 1

Gelatin made from bovine raw materials is safe. There are two fundamental steps to assuring the safety of gelatin: the use of manufacturing processes that have been validated to inactivate BSE infectivity, and the use of safe raw materials.

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The first step – the use of manufacturing processes that assure safety – has been the subject of extensive studies commissioned by the European Commission and GME. These studies were designed to validate that the processes used to manufacture gelatin, as described in the study protocols, are effective at inactivating BSE infectivity. The results of these studies have been presented to regulatory authorities throughout the world. They were presented to FDA's Transmissible Spongiform Encephalopathies Advisory Committee (TSEAC) on July 17, 2003. After thoroughly reviewing the data, the TSEAC concluded that they "demonstrate a reduction in infectivity that is sufficient to protect human health."[1] A summary of the studies used to reach this conclusion is attached as Appendix 1 and complete copies of the studies are provided on the enclosed CD.

The second step – the use of safe raw materials – is accomplished by excluding tissues that may present a significant risk of infectivity. This has been standard Good Manufacturing Practice (GMP) in the gelatin industry for a number of years, and is supported by national regulations. For example, FDA regulations mandate the use of GMP, 21 CFR Part 110; and USDA regulations require the disposal of "specified risk materials" and non-ambulatory disabled cattle (which, under GMP, removes them from the raw material supply for gelatin). 9 CFR §§309.2, 309.3, 310.22, 327.2. In Europe, there are similar requirements: Decision 1999/724/EC on edible gelatin (requirements for raw materials, production and final products), Regulation (EC) No 999/2001 and further amendments on prevention, control and eradication of TSE. All gelatin manufactured by GMIA and GME members is made from safe raw materials. Moreover all raw materials come from animals inspected and passed as fit for human consumption.[2]

As a result of this two-step process, gelatin is safe. As the Scientific Steering Committee of the European Union has stated, these two steps are "considered to be sufficient for the production of safe gelatine."[3]

In its interim final rule, FDA excluded from the definition of "prohibited cattle materials" tallow that contains no more than 0.15 percent hexane-insoluble impurities and tallow derivatives. 21 CFR §§189.5(a)(1), 700.27(a)(1). The effect of this exclusion is to

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[1] Transcript of TSEAC meeting, July 17, 2003, pp. 150, 158. The vote was 7 in favor, 1 abstain, and 1 against.

[2] In addition, we note that bovine hide is recognized as being a safe gelatin raw material without regard to processing conditions in the Terrestrial Animal Health Code (Article 2.3.13.1), and its safety is similarly recognized, provided contamination with potentially infected materials is avoided, in FDA's guidance for industry entitled "The Sourcing and Processing of Gelatin to Reduce the Potential Risk Posed by Bovine Spongiform Encephalopathy (BSE) in FDA-Regulated Products for Human Use" and in the opinion of the Scientific Steering Committee of the European Union referred to in footnote 3 below.

[3] Updated Opinion on the Safety with Regard to TSE Risks of Gelatine derived from Ruminant Bones or Hides, adopted by the Scientific Steering Committee at its Meeting of 6-7 March 2003 (http://europa.eu.int/comm/food/fs/sc/ssc/out321_en.pdf).

exempt tallow that meets this definition, and tallow derivatives, from any of the requirements of the rule. FDA explained the rationale for this exemption as follows:

> "... [T]here is no reason to believe that tallow is likely to contain unusually high amounts of prion protein as a constituent of the insoluble impurities fraction that remains in tallow after rendering. Taylor et al. ... also reported that the various rendering processes used for tallow production in the United Kingdom were sufficient to produce tallow that did not result in infection when injected into the brains of mice, even though the starting material was highly spiked with the scrapie agent. * * * FDA's Transmissible Spongiform Encephalopathy Advisory Committee (TSEAC) considered the safety of tallow and tallow derivatives in 1998.... Members of the Committee indicated that tallow is a food with negligible or no risk of transmitting BSE to humans or animals. * * * Because we believe that tallow has negligible risk of transmitting BSE, and tallow derivatives undergo additional processing, we do not believe that tallow derivatives pose a risk of transmitting the agent that causes BSE to humans." 69 Fed. Reg. 42260-261.

Exactly the same analysis can be applied to gelatin that is made from safe bovine raw materials using manufacturing processes that have been validated to inactivate BSE infectivity. Specifically: (1) such gelatin is unlikely to contain unusually high amounts of prion protein, (2) the manufacturing processes are sufficient to produce a product that does not result in infection when injected into the brains of mice even though the starting material was highly spiked with the infective agent (see the detailed discussion of the gelatin studies at Appendix 1); and (3) the TSEAC considered the safety of gelatin in 2003 and concluded that it is "sufficient to protect human health." Thus gelatin, like exempt tallow and tallow derivatives, is safe. Indeed, we are confident that the data supporting the safety of gelatin are at least as strong as those supporting the safety of tallow.

GMIA and GME believe strongly that gelatin made from safe bovine raw materials using manufacturing processes that have been validated to inactivate BSE infectivity can be and should be exempt from the interim final rule. If necessary, we would be willing to meet with FDA to discuss further the basis for such an exemption.

As a separate issue, it is necessary to ensure that wide varieties of gelatin continue to be readily available and that worldwide sources of safe gelatin and raw materials are not unnecessarily restricted by the interim final rule. To do this, it is necessary to amend FDA's regulation to recognize that cattle products have different levels of BSE risk depending on their geographic origin. Such an amendment is discussed further in Comment 2, below.

COMMENT 2

FDA's requirements for prohibited cattle materials apply to all food and cosmetic products or ingredients of such products imported into the U.S., regardless of source. As a result, the restrictions applicable to high-BSE-risk countries are the same as those for low-BSE-risk countries. For example, FDA's rule prohibits the importation of gelatin made using bone chips from Argentina that include vertebral bone from cattle 30 months and older. However, Argentina is recognized by the Office International des Epizooties (OIE) as provisionally free from BSE,[4] and as a result the risk of BSE presented by cattle materials from Argentina is virtually zero. From a public health perspective, it is not necessary or appropriate to impose such restrictions on cattle products from countries that present a minimal risk, or no risk, of BSE.

The Terrestrial Animal Health Code (the "Code"), administered by the OIE, provides a scientific and regulatory basis for distinguishing between cattle materials from countries with different levels of BSE risk. This Code, which covers various animal diseases in addition to BSE, is intended to help regulatory authorities "avoid the transfer of agents pathogenic for animals or humans, while avoiding unjustified sanitary barriers." The Code has been formally adopted by the OIE International Committee, the general assembly of all Delegates of OIE Member Countries (including the United States). A copy of the relevant portion of the Code (chapter 2.3.13) is attached as Appendix 2.

The Code provides an approach to regulating the importation of cattle products that has broad international agreement among scientists and regulatory authorities. Accordingly, GMIA and GME recommend that FDA amend its regulations to provide for the importation of cattle materials in a manner consistent with the provisions of the Code.

Even if FDA does not adopt the Code provisions for all cattle materials, GMIA and GME recommend strongly that, based on the safety of gelatin (as discussed in Comment 1), FDA amend its regulations to provide for the importation of bovine-origin gelatin (and raw materials intended for use in the manufacture of gelatin) in a manner consistent with the provisions of the Code.

Importantly, although the Code provides a rational, science-based approach to regulating trade in cattle products, many countries have not adopted the use of the Code in their regulation of cattle products imported from the United States. Since January 2004, over 60 foreign countries have prohibited the importation of US bovine products (including bovine bone gelatin for human use) notwithstanding that the US is clearly a low-risk country and has appropriate regulations in place consistent with this level of risk.

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[4] http://www.oie.int/eng/info/en_statesb.htm#evaluation.

Therefore, GMIA and GME recommend that FDA work with other US government agencies and foreign governments to strongly encourage use of the Code as a basis for import regulation. GMIA and GME recommend that FDA only adopt the Code as a basis for regulation of imports of cattle products from countries that also use the Code (or an equivalent standard) as the basis for regulation of imports from the United States.

In addition, GMIA and GME recommend that FDA and USDA adopt a consistent approach to import restrictions. Currently:

- FSIS restricts "specified risk materials," nonambulatory disabled cattle, and certain meat produced by advanced meat recovery systems, and requires foreign establishments shipping meat and meat products to the US to be "equivalent." 9 CFR §327.2.
- APHIS restricts imports of meat and edible products other than meat (excluding certain gelatin, milk, and milk products) from specified countries where BSE exists or that present an "undue risk" of BSE. 9 CFR §94.18(a).
- FDA restricts "prohibited cattle materials" from all countries (including countries that may not be BSE countries under APHIS regulations). 21 CFR §§189.5, 700.27.

Both the public health and the trade in important cattle materials would benefit from revising these rules to be (1) consistent, and (2) based on the Code.

COMMENT 3

The preamble to the interim final rule contains some inaccurate and misleading statements about gelatin. In particular, in explaining why the USDA's rules on specified risk materials may not be adequate to fully protect the food supply, FDA states:

> "The USDA's interim final rule will reduce but will not, by itself, eliminate the availability and use of prohibited cattle materials in domestic and imported FDA-regulated human food and cosmetics. Domestically, generally human food that contains meat only in a relatively small proportion or that historically has not been considered by consumers to be products of the meat food industry (e.g., soup stock, beef flavors and extracts, gelatin), is not produced under USDA inspection (see definition of 'meat food product' in 21 U.S.C. 601(j)) and may be physically available for use in FDA-regulated human food and cosmetics. * * * ... [C]ertain products, such as gelatin and collagen (which are both covered by the provisions of this rule) used in FDA-regulated human food and cosmetics, have traditionally been produced from cattle material deemed inedible by the USDA. Therefore, such a designation by the USDA may not be enough to preclude use of prohibited

cattle materials in FDA-regulated products without additional regulation by FDA." 69 Fed. Reg. 42261.

These statements suggest that gelatin produced from US raw materials may be produced from materials deemed by USDA to be unsafe. This is false: all raw materials procured from US sources used to produce gelatin are from cattle that have been inspected and passed by USDA. As discussed in Comment 1, this is assured by GMP in the gelatin industry and by FDA and USDA regulations. GMIA and GME request that FDA correct and clarify these statements in a Federal Register notice.

COMMENT 4

The preamble to the interim final rule describes FDA's guidance for industry entitled "The Sourcing and Processing of Gelatin to Reduce the Potential Risk Posed by Bovine Spongiform Encephalopathy (BSE) in FDA-Regulated Products for Human Use" (the "Gelatin Guidance"). The preamble states that this guidance recommends, among other things, "that gelatin processors ensure that slaughterhouses that supply cattle bones for gelatin production remove heads, spines, and spinal cords as the first procedure following slaughter." The preamble does not point out, however, that this recommendation only applied to materials from "BSE countries" and countries that "fail to meet OIE standards." (See http://www.fda.gov/opacom/morechoices/industry/guidance/gelguide.htm.) As discussed in Comment 2 above, it is important to distinguish between cattle materials from different geographic locations based on OIE standards – as FDA has itself recognized in its Gelatin Guidance.

COMMENT 5

It is our understanding that the Gelatin Guidance has been superseded by the interim final rule for foods and cosmetics. However, this leaves the Guidance in place for other FDA-regulated products. As explained in our Citizen Petition dated October 20, 2003, the Guidance is worded in such a way that it cannot be literally complied with by EU gelatin manufacturers.[5] Therefore, GMIA and GME strongly recommend that the Gelatin Guidance for FDA-regulated products for oral consumption by humans be (1) eliminated and replaced by the interim final rule (as amended by our comments discussed above), or

[5] Our Citizen Petition explained that the Guidance's requirement that heads, spines, and spinal cords be removed at the slaughterhouse "directly after slaughter" and "as the first procedure following slaughter" must be revised to permit these materials to be removed at any time or place after slaughter. The Petition also explained that the Guidance's requirement that cattle come from "BSE-free herds" must be revised to refer to standards that are in place to evaluate BSE risk in different geographic areas.

(2) harmonized with the interim final rule (reflecting also the intent of our Citizen Petition). If the Gelatin Guidance is not changed in this way, then manufacturers and users of gelatin capsules will potentially need to comply with BOTH the interim final rule and the Gelatin Guidance, because capsules may be used for food (dietary supplement), pharmaceutical, and other FDA-regulated uses. Because the interim final rule and the Gelatin Guidance are inconsistent with each other, this would place an unnecessary regulatory burden on gelatin manufacturers and manufacturers and users of gelatin capsules.

We appreciate your considering these comments. If you have any questions or would like further information, please contact the undersigned.

Respectfully submitted,

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